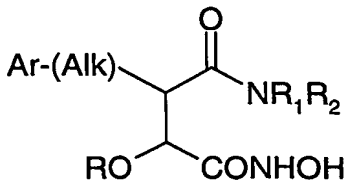
Claims:

1. A compound of formula (I), or an enantiomer or diastereoisomer thereof, or a salt, hydrate or solvate thereof:



(I)

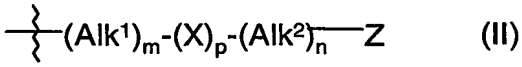
wherein

Ar represents an optionally substituted aryl, heteroaryl, C_3-C_8 cycloalkyl or heterocycloakyl group;

R represents hydrogen or C_1-C_6 alkyl, or C_3-C_6 cycloalkyl;

Alk represents a divalent C_1-C_5 alkylene or C_2-C_5 alkenylene radical; and

R_1 and R_2 taken together with the nitrogen atom to which they are attached form a first heterocycloalkyl ring which is optionally fused to a second C_3-C_8 cycloalkyl or heterocycloalkyl ring, the said first and second rings being optionally substituted by at least one group of formula (II):



(II)

wherein

m, p and n are independently 0 or 1;

Z represents, hydrogen, or an optionally substituted carbocyclic or heterocyclic ring of from 5 to 7 ring atoms which is optionally fused to another optionally substituted carbocyclic or heterocyclic ring of from 5 to 7 ring atoms;

Alk^1 and Alk^2 independently represent optionally substituted divalent C_1-C_3 alkylene radicals;

X represents -O-, -S-, -S(O)-, -$S(O_2)$-, -C(=O)-, -NH-, -NR_3-, -$S(O_2)NH$-, -$S(O_2)NR_3$-, -$NHS(O_2)$-, or -$NR_3S(O_2)$-, where R_3 is C_1-C_3 alkyl.

2. A compound as claimed in claim 1 wherein R is hydrogen.

3. A compound as claimed in claim 1 wherein R is methyl.

4. A compound as claimed in claim 1 wherein R is ethyl, n-propyl, isopropyl, n-, sec- or tert-butyl, cyclopropyl, or cyclopentyl.

5. A compound as claimed in any of the preceding claims wherein Ar is a 5- or 6- membered monocyclic aryl or heteroaryl ring, which is optionally substituted by at least one substituent selected from (C_1-C_3)alkyl, (C_1-C_3)alkoxy, hydroxy, hydroxy(C_1-C_3)alkyl, mercapto, mercapto(C_1-C_3)alkyl, (C_1-C_3)alkylthio, halo, trifluoromethyl, trifluoromethoxy, nitro, nitrile (-CN), -COOH, -$COOR^A$, -COR^A,-SO_2R^A, -$CONH_2$, -SO_2NH_2, -$CONHR^A$, -SO_2NHR^A, -$CONR^AR^B$, -$SO_2NR^AR^B$, -NH_2, -NHR^A, -NR^AR^B, -$OCONH_2$, -$OCONHR^A$, -$OCONR^AR^B$, -$NHCOR^A$, -$NHCOOR^A$, -NR^BCOOR^A, -$NHSO_2OR^A$, -$NR^BSO_2OR^A$, -$NHCONH_2$, -NR^ACONH_2, -$NHCONHR^B$, -NR^ACONHR^B, -$NHCONR^AR^B$, or -$NR^ACONR^AR^B$ wherein R^A and R^B are independently C_1-C_3 alkyl, phenyl or a 5- or 6-membered monocyclic aryl or heteroaryl ring.

6. A compound as claimed in claim 5 wherein an optional substituent is in the 4- position in the case of a 6-membered ring, or in the 2- and/or 3- position in the case of a 5-membered ring.

7. A compound as claimed in any of the preceding claims wherein Ar is optionally substituted phenyl, 2-, 3-, or 4-pyridyl, 2-, or 3-thienyl, or 2-, or 3-furanyl.

8. A compound as claimed in any of the preceding claims wherein optional substituents in Ar are selected from methoxy, ethoxy,

trifluoromethoxy, methyl, ethyl, trifluoromethyl, hydroxyl, mercapto, fluoro, chloro, and bromo.

9. A compound as claimed in claim 5 wherein Ar is 4-(C_1C_3alkoxy)phenyl.

10. A compound as claimed in claim 5 wherein Ar is 4-ethoxyphenyl

11. A compound as claimed in any of the preceding claims wherein Alk is $-CH_2-$, $-CH_2CH_2-$, $-CH_2CH(CH_3)-$, $-CH_2CH_2CH_2-$, $-CH_2CH_2CH_2CH_2-$, $-CH=CH-$, $-CH_2CH=CH-$, $-CH_2CH=CHCH_2-$, or $-CH=CHCH=CH-$.

12. A compound as claimed in any of the preceding claims wherein $-NR_1R_2$ forms a pyrrolidinyl, morpholyl, or thiomorpholyl ring

13. A compound as claimed in any of claims 1 to 11 wherein $-NR_1R_2$ forms a piperidinyl, or piperazinyl ring

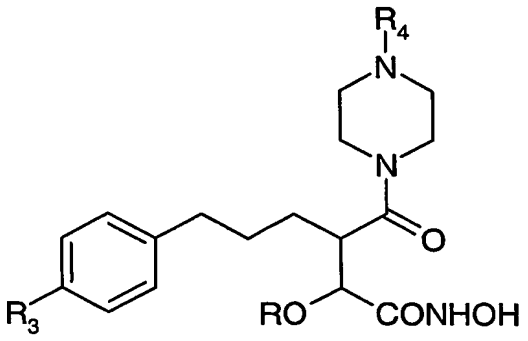
14. A compound as claimed in any of the preceding claims wherein in the group (II), when present, p is 0, Z is hydrogen and at least one of n and m is 1.

15. A compound as claimed in any of claims 1 to 13 wherein in the group (II), when present, m, n and p are all 0 and Z is a carbocyclic or heterocyclic ring directly linked to a ring carbon or ring nitrogen of the $-NR_1R_2$ group.

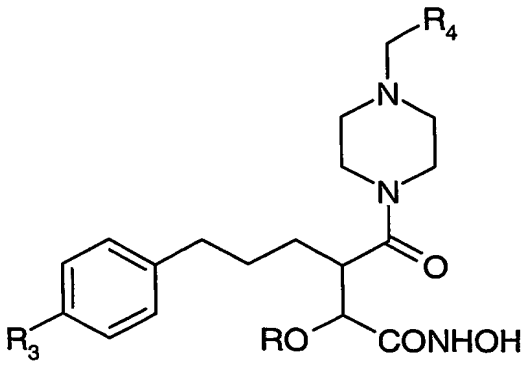
16. A compound as claimed in any of claims 1 to 13 wherein in the group (II), when present, p is 0, at least one of m and n is 1, and Z is a carbocyclic or heterocyclic ring linked to a ring carbon or ring nitrogen of the $-NR_1R_2$ group via a C_1-C_6 alkylene linker between Z and the $-NR_1R_2$ ring.

17. A compound as claimed in any of claims 1 to 13 wherein in the group (II), when present, p is 1.

18. A compound as claimed in claim 1 of formula (IB) or (IC) or an enantiomer or diastereoisomer thereof, or a salt, hydrate or solvate thereof:



(IB)

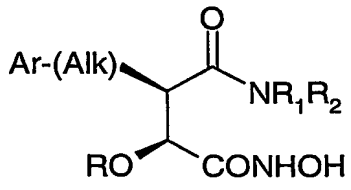


(IC)

wherein R is hydrogen or methoxy, R_3 is trifluoromethyl, trifluoromethoxy C_1-C_3alkoxy, hydroxy, or halo; R_4 is (i) $-SO_2R_5$ or $-COR_5$ wherein R_5 is C_1-C_6alkyl or phenyl or monocyclic heteroaryl having 5 or 6 ring atoms, optionally substituted by (C_1-C_3)alkyl, (C_1-C_3)alkoxy, hydroxy, hydroxy(C_1-C_3)alkyl, mercapto, mercapto(C_1-C_3)alkyl, (C_1-C_3)alkylthio, halo, trifluoromethyl, trifluoromethoxy or (ii) phenyl or monocyclic heteroaryl having 5 or 6 ring atoms; optionally substituted by (C_1-C_3)alkyl, (C_1-C_3)alkoxy, hydroxy, hydroxy(C_1-C_3)alkyl, mercapto, mercapto(C_1-C_3)alkyl, (C_1-C_3)alkylthio, halo, trifluoromethyl, trifluoromethoxy.

19. A compound as claimed in claim 18 wherein a heteroaryl ring forming part of R_4 is pyridyl, pyrimidinyl, triazinyl, thienyl, or furanyl.

20. A compound as claimed in any of the preceding claims having the stereochemical configuration shown in formula (IA):



(IA)

21. A compound as claimed in claim 1, which is selected from the group consisting of:

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-(pyrrolidine-1-carbonyl)-hexanoic acid hydroxyamide.

3R-(6,7-dimethoxy-3,4-dihydro-1H-isoquinoline-2-carbonyl)-6-(4-ethoxy-phenyl)-2S-hydroxy-hexanoic acid hydroxyamide.

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-[4-(3-methoxy-phenyl)-piperazine-1-carbonyl]-hexanoic acid hydroxyamide.

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-[4-(4-methoxy-phenyl)-piperazine-1-carbonyl]-hexanoic acid hydroxyamide.

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-(4-pyridin-2-yl-piperazine-1-carbonyl)-hexanoic acid hydroxyamide.

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-(4-pyridin-4-yl-piperazine-1-carbonyl)-hexanoic acid hydroxyamide.

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-(morpholine-4-carbonyl)-hexanoic acid hydroxyamide.

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-(2RS-methyl-morpholine-4-carbonyl)-hexanoic acid hydroxyamide.

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-(2,6-RS-dimethyl-morpholine-4-carbonyl)-hexanoic acid hydroxyamide.

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-(thiomorpholine-4-carbonyl)-hexanoic acid hydroxyamide.

3R-(4-benzyl-piperidine-1-carbonyl)-6-(4-ethoxy-phenyl)-2S-hydroxy-hexanoic acid hydroxyamide.

3R-(4-benzo[1,3]dioxol-5-ylmethyl-piperazine-1-carbonyl)-6-(4-ethoxy-phenyl)-2S-hydroxy-hexanoic acid hydroxyamide.

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-(4-pyridin-4-ylmethyl-piperazine-1-carbonyl)-hexanoic acid hydroxyamide.

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-(4-benzylpiperazine-1-carbonyl)-hexanoic acid hydroxyamide.

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-(4-pyrimidin-2-yl-piperazine-1-carbonyl)-hexanoic acid hydroxyamide.

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-[4-(4-trifluoromethyl-pyrimidin-2-yl)-piperazine-1-carbonyl]-hexanoic acid hydroxyamide.

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-[4-(4-chloro-pyrimidin-2-yl)-piperazine-1-carbonyl]-hexanoic acid hydroxyamide.

3R-[4-(4,6-dimethoxy-[1,3,5]triazin-2-yl)-piperazine-1-carbonyl]-6-(4-ethoxy-phenyl)-2S-hydroxy-hexanoic acid hydroxyamide.

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-[4-(3-trifluoromethyl-phenyl)-piperazine-1-carbonyl]-hexanoic acid hydroxyamide.

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-[4-(2-fluoro-phenyl)-piperazine-1-carbonyl]-hexanoic acid hydroxyamide.

3R-[4-(acetyl-methyl-amino)-piperidine-1-carbonyl]-6-(4-ethoxy-phenyl)-2S-hydroxy-hexanoic acid hydroxyamide.

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-[4-(methyl-propyl-amino)-piperidine-1-carbonyl]-hexanoic acid hydroxyamide.

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-(3S-benzyl-morpholine-4-carbonyl)-hexanoic acid hydroxyamide.

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-(3S-isobutyl-morpholine-4-carbonyl)-hexanoic acid hydroxyamide.

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-(3S-phenyl-morpholine-4-carbonyl)-hexanoic acid hydroxyamide.

3R-(4-benzyl-3RS-methyl-piperazine-1-carbonyl)-6-(4-ethoxy-phenyl)-2S-hydroxy-hexanoic acid hydroxyamide.

3R-(3S,4-dibenzyl-piperazine-1-carbonyl)-6-(4-ethoxy-phenyl)-2S-hydroxy-hexanoic acid hydroxyamide.

3R-(4-benzyl-3RS-phenyl-piperazine-1-carbonyl)-6-(4-ethoxy-phenyl)-2S-hydroxy-hexanoic acid hydroxyamide.

4-(4-benzo[1,3]dioxol-5-ylmethyl-piperazin-1-yl)-2S,N-dihydroxy-4-oxo-3R-(4-trifluoromethoxy-benzyl)-butyramide.

3R-benzyl-2S,N-dihydroxy-4-morpholin-4-yl-4-oxo-butyramide.

3R-(4-Benzyloxy-benzyl)-2S,N-dihydroxy-4-oxo-4-piperidin-1-yl-butyramide.

2S,N-dihydroxy-3R-(4-hydroxy-benzyl)-4-oxo-4-piperidin-1-yl-butyramide.

4-(4-benzo[1,3]dioxol-5-ylmethyl-piperazin-1-yl)-3R-(4-benzyloxy-benzyl)-2S,N-dihydroxy-4-oxo-butyramide.

6-(3,5-bis-trifluoromethyl-phenyl)-2S-hydroxy-3R-(morpholine-4-carbonyl)-hexanoic acid hydroxyamide.

3R-(4-benzyl-piperidine-1-carbonyl)-6-(3,5-bis-trifluoromethyl-phenyl)-2S-hydroxy-hexanoic acid hydroxyamide.

6-(3,5-bis-trifluoromethyl-phenyl)-2S-hydroxy-3R-(4-pyridin-2-yl-piperazine-1-carbonyl)-hexanoic acid hydroxyamide.

6-(3,5-bis-trifluoromethyl-phenyl)-3R-(6,7-dimethoxy-3,4-dihydro-1H-isoquinoline-2-carbonyl)-2S-hydroxy-hexanoic acid hydroxyamide.

6-(3,5-bis-trifluoromethyl-phenyl)-2S-hydroxy-3R-(pyrrolidine-1-carbonyl)-hexanoic acid hydroxyamide

3R-(2S-benzyl-4-methyl-piperazine-1-carbonyl)-6-(4-ethoxy-phenyl)-2S-hydroxy-hexanoic acid hydroxyamide.

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-[4-(4-trifluoromethoxy-benzenesulfonyl)-piperazine-1-carbonyl]-hexanoic acid hydroxyamide.

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-[4-(toluene-4-sulfonyl)-piperazine-1-carbonyl]-hexanoic acid hydroxyamide.

3R-[4-(5-bromo-thiophene-2-sulfonyl)-piperazine-1-carbonyl]-6-(4-ethoxy-phenyl)-2S-hydroxy-hexanoic acid hydroxyamide.

3R-[4-(5-benzenesulfonyl-thiophene-2-sulfonyl)-piperazine-1-carbonyl]-6-(4-ethoxy-phenyl)-2S-hydroxy-hexanoic acid hydroxyamide.

3R-[4-(4-butoxy-benzenesulfonyl)-piperazine-1-carbonyl]-6-(4-ethoxy-phenyl)-2S-hydroxy-hexanoic acid hydroxyamide.

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-[4-(4-methoxy-2,3,6-trimethyl-benzenesulfonyl)-piperazine-1-carbonyl]-hexanoic acid hydroxyamide.

3R-[4-(3,4-dimethoxy-benzenesulfonyl)-piperazine-1-carbonyl]-6-(4-ethoxy-phenyl)-2S-hydroxy-hexanoic acid hydroxyamide.

6-(4-methoxy-phenyl)-2S-hydroxy-3R-[4-(2-fluoro-phenyl)-piperazine-1-carbonyl]-hexanoic acid hydroxyamide.

6-(4-methoxy-phenyl)-2S-hydroxy-3R-(4-pyridin-2-yl-piperazine-1-carbonyl)-hexanoic acid hydroxyamide.

6-(4-fluoro-phenyl)-3R-[4-(2-fluoro-phenyl)-piperazine-1-carbonyl]-2S-hydroxy-hexanoic acid hydroxyamide.

6-(4-fluoro-phenyl)-2S-hydroxy-3R-(4-pyridin-2-yl-piperazine-1-carbonyl)-hexanoic acid hydroxyamide.

3R-(4-benzyl-2S-methyl-piperazine-1-carbonyl)-6-(4-ethoxy-phenyl)-2S-hydroxy-hexanoic acid hydroxyamide.

3R-(4-benzyl-2S-methyl-piperazine-1-carbonyl)-6-(4-methoxy-phenyl)-2S-hydroxy-hexanoic acid hydroxyamide.

3R-(4-benzyl-2S-i-butyl-piperazine-1-carbonyl)-6-(4-methoxy-phenyl)-2S-hydroxy-hexanoic acid hydroxyamide.

3R-(4-benzyl-2S-methyl-piperazine-1-carbonyl)-6-(4-fluoro-phenyl)-2S-hydroxy-hexanoic acid hydroxyamide.

3R-(4-benzyl-2S-i-butyl-piperazine-1-carbonyl)-6-(4-fluoro-phenyl)-2S-hydroxy-hexanoic acid hydroxyamide.

4-[5-(4-ethoxy-phenyl)-2R-(1S-hydroxy-hydroxycarbamoyl-methyl)-pentanoyl]-2S-methyl-piperazine-1-carboxylic acid tert-butyl ester.

4-[5-(4-ethoxy-phenyl)-2R-(1S-hydroxy-hydroxycarbamoyl-methyl)-pentanoyl]-2S-i-butyl-piperazine-1-carboxylic acid tert-butyl ester.

4-[5-(4-methoxy-phenyl)-2R-(1S-hydroxy-hydroxycarbamoyl-methyl)-pentanoyl]-2S-methyl-piperazine-1-carboxylic acid tert-butyl ester.

4-[5-(4-methoxy-phenyl)-2R-(1S-hydroxy-hydroxycarbamoyl-methyl)-pentanoyl]-2S-i-butyl-piperazine-1-carboxylic acid tert-butyl ester.

4-[5-(4-fluoro-phenyl)-2R-(1S-hydroxy-hydroxycarbamoyl-methyl)-pentanoyl]-2S-methyl-piperazine-1-carboxylic acid tert-butyl ester.

4-[5-(4-fluoro-phenyl)-2R-(1S-hydroxy-hydroxycarbamoyl-methyl)-pentanoyl]-2S-i-butyl-piperazine-1-carboxylic acid tert-butyl ester,

6-(4-ethoxy-phenyl)-2S-methoxy-3R-[4-(2-fluoro-phenyl)-piperazine-1-carbonyl]-hexanoic acid hydroxyamide.

22. A pharmaceutical composition comprising a compound as claimed in any of the preceding claims, together with a pharmaceutically acceptable carrier.

23. A compound as claimed in any of claims 1 to 21 for use as a medicament.

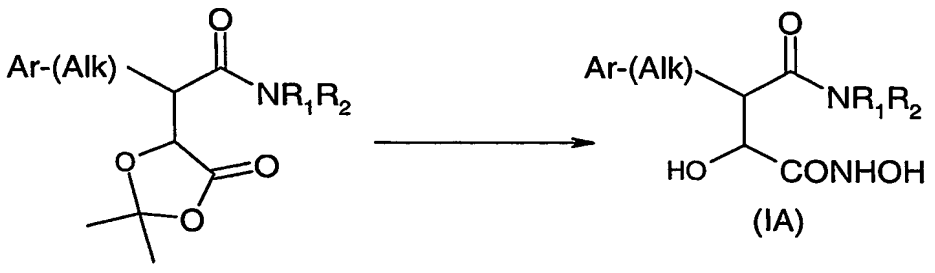
24. A method of treatment or prophylaxis of diseases or conditions responsive to inhibition of MMP-12 and/or MMP-9 in mammals, which method comprises administering to the mammal an effective amount of a compound as claimed in any of claims 1 to 21

25 The use of a compound as claimed in any of claims 1 to 21 in the preparation of an agent for the treatment or prophylaxis of diseases or conditions responsive to inhibition of MMP-12 and/or MMP-9.

26. A method as claimed in claim 24 or a use as claimed in claim 25 wherein the disease or condition is bone resorption, tumour growth or invasion by secondary metastases; rheumatoid arthritis, septic arthritis, osteoarthritis, periodontitis, gingivitis, corneal ulceration, cardiac hypertrophy, acute respiratory distress syndrome, neuroinflammatory disorders, e.g. multiple sclerosis; restenosis; emphysemia; fibrotic didease e.g. fibrosis post radiotherapy, kerotid scarring, liver fibrosis and cystic fibrosis; chronic obstructive pulmonary disease; bronchitis; asthma; autoimmune disease; transplant rejection (e.g. graft versus host disease); cystic fibrosis; psoriasis; psoriatic arthritis; degenerative cartilage loss; inflammatory gastric conditions, e.g. Crohn's disease, inflammatory bowel disease, and ulcerative colitis; atopic dermatitis, epidermolysis bullosa; epidermic ulceration; a neuropathy or nephropathy e.g.interstitial nephritis, glomerulonephriris or renal failure; ocular inflammation; liver cirrhosis, Sjoegren's syndrome; or an inflammatory condition of the nervous system.

27. A method as claimed in claim 24 or a use as claimed in claim 25 wherein the disease or condition is fibrotic disease, multiple sclerosis, emphysemia, bronchitis or asthma.

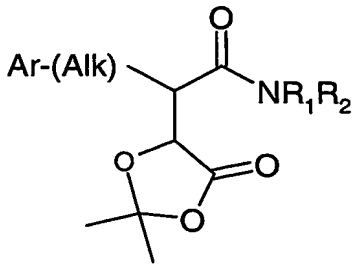
28. A method of preparing metalloproteinase inhibitors of formula (IA) according to any of claims 1 to 21 wherein R is hydrogen, comprising the de-protection and/or transformation step of:



(IIIB) (IA)

wherein Ar, Alk, R_1 and R_2 are as defined in any of claims 1 to 16.

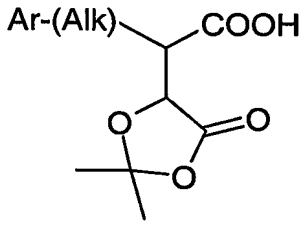
29. A compound of formula (IIIB)



(IIIB)

wherein Ar, Alk, R_1 and R_2 are as defined in any of claims 1 to 19.

30. A process for the preparation of a compound as claimed in claim 29 comprising comprising the step of reacting a compound of formula (III)



(III)

with a cyclic amine HNR_1R_2., wherein Ar, Alk, R_1 and R_2 are as defined in any of claims 1 to 19.